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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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09/902,853

07/10/2001

Avi Ashkenazi

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35489

7590

01/16/2004

EXAMINER

SPECTOR, LORRAINE

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275 MIDDLEFIELD ROAD
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ART UNIT

PAPER NUMBER

1647

DATE MAILED: 01/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/902,853	Applicant(s) ASHKENAZI ET AL.	
	Examiner Lorraine Spector, Ph.D.	Art Unit 1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 39-44 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 39-44 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 a) ☐ All b) ☐ Some * c) ☐ None of:
 1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. ____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
 a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). ____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) ____ | 6) <input type="checkbox"/> Other: |

Part III: Detailed Office Action

Claims 39-44 are pending and under consideration.

Formal Matters:

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

The disclosure is objected to because of the following informalities:

Applicants are advised that the ATCC has moved from Rockville, MD to Manassas, VA, effective March 23, 1998. The correct address is now:

American Type Culture Collection
10801 University Boulevard
Manassas, VA 20110-2209

Appropriate correction is required.

IDS:

The information disclosure statement, filed 3/25/2002, has been considered. The BLAST results demonstrate that applicants are aware of proteins with identity/homology to the one claimed herein. However, as the BLAST results do not give sufficient identifying information, the Examiner cannot determine if said sequences constitute prior art.

Priority Determination:

The disclosed antibodies have no utility; see rejection, below. Accordingly, for the purposes of applying prior art, the effective filing date of this application is its actual filing date, 7/10/2001.

Objections and Rejections under 35 U.S.C. §101 and §112:

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 39-44 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific, substantial and credible asserted utility or a well established utility.

The claims are directed to antibodies that bind to the protein of SEQ ID NO: 259. The specification contains numerous asserted utilities including use, to identify molecules that bind to PRO (including agonists and antagonists), as molecular weight markers, therapeutic agents, and for the production of antibodies. The utilities that pertain solely to nucleic acids (e.g. hybridization, chromosome and gene mapping, anti-sense) would not convey to the encoded protein or antibodies that bind thereto. With respect to the remaining utilities, none of these asserted utilities is specific for the disclosed PRO304 protein or antibodies, as each of the aforementioned utilities could be asserted for any naturally occurring protein, and further, as none of the asserted utilities requires any feature or activity that is specific to the disclosed PRO304.

The specification teaches that PRO304 has (unspecified) homology to unspecified "various protease enzymes, for example see page 29 or page 40. The structure of the putative PRO304 peptide is not discussed in the specification; there is no disclosure that the protein is expected to be a transmembrane protein, nor of any extracellular domain. There is no biological activity, expression pattern, phenotype, disease or condition, ligand, binding partner, or any other specific feature that is disclosed as being associated with PRO304. Without any information as to the specific properties of PRO304, the mere identification of such as having homology to various proteases is not sufficient to impart any particular utility to the claimed polypeptides, and hence to the antibodies that bind thereto.

Even though the data demonstrated a slight increase in copy number of PRO304 nucleic acids in primary lung squamous cell carcinoma cells (see pages 222-225 of the specification),

such is not be indicative of a use of the encoded polypeptide as a diagnostic agent. Cancerous tissue is known to be aneuploid, that is, having an abnormal number of chromosomes (see Sen, 2000, Curr. Opin. Oncol. 12:82-88). A slight amplification of a gene does not necessarily mean overexpression in a cancer tissue, but can merely be an indication that the cancer tissue is aneuploid. The preliminary data were not supported by analysis of mRNA or protein expression, for example. Thus, the data do not support the implicit assertion that PRO304 can be used as a cancer diagnostic. Significant further research would have been required of the skilled artisan to determine whether PRO304 is overexpressed in any cancer to the extent that it could be used as a cancer diagnostic, and thus the implicitly asserted utility is not substantial.

A patent is granted for a completed invention, not the general suggestion of an idea and how that idea might be developed into the claimed invention. In the decision of *Genentech, Inc. v. Novo Nordisk*, 42 USPQ 2d 100, (CAFC 1997), the court held that:

“[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable” and that “[t]ossing out the mere germ of an idea does not constitute enabling disclosure”. The court further stated that “when there is no disclosure of any specific starting material or of any of the conditions under which a process is to be carried out, undue experimentation is required; there is a failure to meet the enablement requirements that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art”, “[i]t is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement”.

The instant specification provides the sequence of a protein, and then goes on to invite the reader to find out what the biological significance of the protein is, with suggestions as to what ‘might’ be. There is not credible correlation of the protein with any real world, available use, nor, by extension is there any real world use for the claimed antibodies. The instant specification lacks utility and is not enabling because one cannot, following the guidance presented therein, practice the suggested method without first making a substantial inventive contribution.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 39-44 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 44 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 39 states that the claimed antibody "binds" the protein of SEQ ID NO: 12, whereas dependent claim 44 states that the antibody "specifically binds". The term "specifically" in claim 44 is a relative term which renders the claim indefinite. The term "specifically" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Rejections Over Prior Art:

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for

patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 39-44 are rejected under 35 U.S.C. 102(e) as being anticipated by Lobel et al., U.S. Patent Number 6,302,685.

Lobel et al a human lysosomal pepstatin-insensitive protease. The amino acid sequence of SEQ ID NO: 3 therein is 99.8% identical to residues 1-551 of SEQ ID NO: 259. Antibodies are discussed at columns 18-20 and include monoclonal, humanized, fragment, and labelled antibodies. Accordingly, the invention is anticipated by Lobel et al.

Claims 39 and 44 are rejected under 35 U.S.C. 102(b) and (e) as being anticipated by Jacobs et al., U.S. Patent Number 5,831,056.

Jacobs et al. disclose a protein of SEQ ID NO: 2, which is 100% identical to residues 1-85 of SEQ ID NO: 259. Antibodies, including both monoclonal and polyclonal antibodies, are disclosed at column 22, lines 44-65. The therapeutic use of such antibodies, implicitly for humans, is also disclosed.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 43 is rejected under 35 U.S.C. 103(a) as being unpatentable over Jacobs et al.

As stated above, Jacobs et al. teach antibodies to their protein. They further state that the antibodies can be used in detection of cancer. Jacobs et al. do not specifically disclose that antibodies used in detection are 'labelled'. However, the production of labeled antibodies is considered obvious over Jacobs et al., as the practice of labeling antibodies to allow detection of such is notoriously old and well known in the art, and would be immediately envisaged by the person of ordinary skill in the art upon reading the Jacobs et al. disclosure.

Claims 41 and 42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jacobs et al., as cited in the above rejection under 35 U.S.C. § 102(b) and (e), in view of U.S. Patent Number 5,565,332 (Hoogenboom et al.) in the case of claim 41, or in view of U.S. Patent Number 4,946,778 (Ladner et al.) in the case of claim 42.

Claims 40-43 contain the additional limitation that the claimed antibodies are humanized, or a fragment of an antibody. It cannot be determined whether Yoshida et al. teach such (no translation from the Japanese was available at the time this Office Action was written).

Hoogenboom et al. disclose humanized antibodies and methods of making such. At col. 1 lines 16-30 they disclose the advantages of such as being overcoming the problem of elicitation of anti-globulin response when a non-human antibody is administered to a human. See also col. 3 lines 8-15 in this regard. At column 2 lines 57+, they disclose that antibody fragments can perform the function of whole antibodies, and set forth single chain antibodies as being examples of antibody fragments.

Ladner et al. teach the construction of single chain antibodies. The stated advantages of such as enumerated at column 3 lines 32-48 include smaller size, greater stability, lower cost, lower immunogenicity, etc.

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to substitute the antibodies of Jacobs et al. into the single chain or humanized antibodies of Ladner et al. or Hoogenboom et al. to attain the known and expected

advantages of such as set forth by the secondary references and as referred to above. It is noted that a single chain antibody is considered additionally to be an 'antibody fragment', as disclosed by Hoogenboom et al.

Accordingly, the invention, in view of the prior art, is *prima facie* obvious.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Sleat et al., Science 277 :1802-1805, 1997, teach a human lysosomal pepstatin-insensitive protease. The nucleic acid sequence therein encodes a protein 99.8% identical to residues 1-551 of SEQ ID NO: 259, see attached alignment. They further teach that mutations in the protein, and hence the nucleic acid encoding it, are associated with classical late-infantile neuronal ceroid lipofuscinosis. The protein shown in Figure 1 is isolated.

Advisory Information:

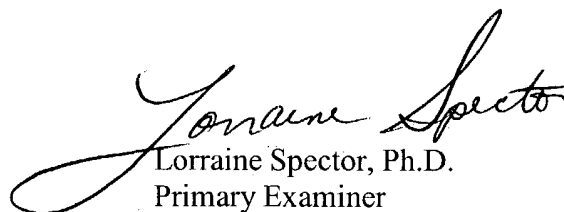
Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Lorraine M. Spector, whose telephone number is (703) 308-1793. Dr. Spector can normally be reached Monday through Friday, 9:00 A.M. to 5:30 P.M. ***Effective 1/21/2004, Dr. Spector's telephone number will be 571-272-0893.***

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Dr. Gary L. Kunz, at (703)308-4623. ***Effective 1/21/2004, Dr. Kunz' telephone number will be 571-272-0887.***

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist at telephone number (703) 308-0196.

Certain papers related to this application may be submitted to Group 1800 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). NOTE: If Applicant does submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Official papers filed by fax should be directed to (703) 872-9306 (before final rejection) or (703) 872-9307 (after final). Faxed draft or informal communications with the examiner should be directed to (703) 746-5228. *Effective 1/21/2004, Dr. Spector's fax number will be 571-273-0893.*


Lorraine Spector, Ph.D.
Primary Examiner